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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,396	07/10/2001	Keith D. Allen	R-359	9463

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,396	ALLEN, KEITH D.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-41,47 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-41,47 and 48* is/are rejected.

7)☐ Claim(s) *47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08/15/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/08/2005 has been entered.

Claims 1-35 and 42-46 have been cancelled. Claims 36-41,47 and 48 are pending and under consideration in the instant office action.

Claim Objections

Claim 47 is objected to because of the following informalities: Claim 47 requires that a pseudopregnant mouse give birth. However, a pseudopregnant mouse is not pregnant and cannot give birth. Appropriate correction is required.

Claim Rejections - 35 USC § 101/112

Utility

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to

a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

See also the MPEP § 2107 - 2107.02.

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-41,47 and 48 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The rejection set forth on pages 2-9 of the previous office action mailed 09/09/2004 is maintained for reasons of record.

The instant specification has discussed that the mice of the instant invention can be used as models of disease to screen for drug therapies and as a tool for studying the function of a glucocorticoid-induced receptor gene. As set forth in the previous office action, these uses fail to meet the standards of a specific, substantial and well-established utility required under 35 U.S.C. 101. In summary, the utilities provided by Applicant for the claimed mouse are not specific or

substantial and therefore are not well established because the use of the mouse in screening for drugs to treat an unknown disease is not specific. The use for the claimed mouse in characterizing the function of a glucocorticoid-induced receptor gene is not substantial. The basis for this rejection is further set forth in the previous office action and in the guidelines above.

Applicant has argued that the Patent Office guidelines state that a rejection for lack of utility may not be imposed where an invention has a well-established utility or is useful for any particular practical purpose (first 6 pages of Applicant's Remarks; pages are not numbered). Applicant cites excerpts from an NIH website, Albert, Austin et al., 2004 and Lewin's Genes VII in establishing that knockout mice are invaluable tools of scientific research. Applicant also cites the MPEP in discussing the utility of research tools (pages 8 of Applicant's response; MPEP 2107.01, I). Applicant submits that one of ordinary skill in the art would readily recognize the utility of a knockout mouse in studying gene function (7th page of Remarks). In general, Applicant does not understand how the invention cannot have utility when the invention is being used by one of skill in the art and has clearly been accepted as useful by several leaders in the field of transgenic technology.

In response, the instant invention has failed to meet the requirements of possessing a well-established utility and for a use with any particular practical purpose. A well-established utility and a utility with a particular practical purpose is one that is specific and substantial (see MPEP 2107(II)(A)(3)(ii) and MPEP 2107 (II)(B)(1)). The utility of the instant invention is neither specific nor substantial for reasons of record. Applicant is reminded that the utility guidelines (see above) expressly state that utilities requiring further research to identify or reasonably confirm a use do not define substantial utilities. Examples of uses that are not

considered substantial utilities include basic research in studying the claimed product and use to screen for therapeutics for an unspecified disease. The use of the invention by the skilled artisan does not impart patentability or patentable use on the invention for reasons set forth above.

With specific respect to Applicant's applied references, the validity of the opinion of the NIH, Ben Lewin and Austin et al. with respect to the value of the knockout mouse in determining gene function is not questioned. However, the use of a mouse to determine gene function, as set forth above, does not meet the requirement that a utility be specific and substantial, and therefore, does not fulfill the requirements of utility under 35 USC 101. With respect to MPEP 2107.01, I, a gas chromatograph is a research tool with a well-defined function and highly specific use that does not necessitate further study of itself. It may be that a gas chromatograph may be used for a wide variety of analyses; however, this does not change its specific use for analyzing a sample. In contrast, the claimed invention is not a general tool for analyzing other samples and, at most, serves to study the function of a single gene. In this respect, the utility of a knockout mouse cannot be compared to a gas chromatograph. Therefore, the utility of the instant invention is neither specific nor substantial.

Applicant also discloses the commercial use of the claimed mice and states that commercial use and acceptance is one important indication that the utility of an invention has been recognized by one of skill in the art (page 8 of Applicant's remarks).

In response, Applicant fails to provide description or evidence of any commercial use. Applicant has not provided any evidence pertaining to what the mice would be used for if sold and therefore, without evidence to the contrary, it is assumed that the mice are being used for the uses of record, namely in screening for drugs to treat a non-specified disease, in studying gene

function and in studying gene expression (see below). As set forth above and in the previous office action, theses uses are not specific or substantial. Applicant is reminded that the requirements under §101 and §112, 1st para. must be met at the time the application is filed. The discovery of a use meeting these requirements after the application is filed does not satisfy the statutory requirements under either §101 or §112, 1st para. See *In re Kirk*, 153 USPQ 48, 52 (CCPA 1967); *In re Wright*, 27 USPQ2d 1510, 1514 (Fed. Cir. 1993).

Applicant has referred to the principles set forth in *In re Brana* (see pages 8-10 of Applicant's remarks). Applicant asserts that the specification supports a use of the knockout mouse that is specific and substantial in light of the teaching of *In re Brana.*

In response, the fact pattern in *Brana* does not correlate to the fact pattern of the instant application. In *Brana*, the court addressed two separate issues, utility and enablement. The court held that the specification did, in fact, disclose a specific and substantial use for the compound, treating leukemia, and that this use was overlooked by the PTO in making the rejection under 101. The court observed that the claimed compound was similar in structure to compounds in the prior art that were useful in treating leukemia. The claimed compound behaved in a manner similar to that of the prior art in art accepted assays for anti-leukemic activity. Therefore, the specification enabled the use. The instant specification and the art of record fail to support such a patentable utility for the instant invention and therefore, the principles set forth in *In re Brana* do not apply to the instant invention.

Applicant argues that the mice are useful in studying the association of the glucocorticoid-induced receptor gene function with respect to its role in depression and hyperactivity (9th page of Applicant's Remarks).

In response, this argument is similar to that set forth above. For reasons set forth in the Final Office Action mailed 09/09/2004, the specification fails to establish a link between the claimed gene disruption and hyperactivity or depression (see pages 3-8). Without a clear link, it would require additional experimentation to confirm this link, which renders the utility of the mouse as not substantial until such a correlation is made. The specification fails to clearly establish that the claimed mouse is means of studying hyperactivity or depression. The study of how the glucocorticoid-induced receptor affects hyperactivity and depression is not substantiated or supported by the teachings in the specification and is not a patentable utility because the requirement for further research is not a substantial use as defined by the utility guidelines se forth above.

In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse and cells encompassed by the claims to be specific and substantial.

Enablement

Claims 36-41,47 and 48 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following issue of enablement must also be addressed:

The rejection of the claims respect to the breadth of the claims regarding the genetic background of the claimed mice is maintained as set forth on pages 9-10 of the previous office action mailed 09/09/2004. The grounds of the rejection is based on the differences reported in phenotype of the claimed mice depending on the genetic background.

Applicant argues subject matter sought to be patented must be taken as in compliance with the enablement requirement unless there is reason to doubt the objective truth. Applicant argues that an insertional gene disruption, should, as a general rule, result in a null allele or ablation of gene function. Applicant states, "Ablation of gene function is expected to result in the same phenotypic response." Applicant asserts that the Examiner has not provided any evidence to the contrary. Finally, Applicant presents the teachings of Bilkie-Gorzo as an example where genetic background does not affect phenotypic manifestation of a genetic disruption.

In response, this argument is unclear. First, Applicant is not correct in asserting that any insertional disruption will result in a null allele because the site if insertion is crucial in determining the effect on gene function. Second, it is not clear what Applicant is arguing. It appears as though Applicant is arguing reproducibility of phenotype of various null insertional mutations because Applicant does not set forth what groups of mice are expected to have "the same phenotypic response". Finally, with respect to the assertion that the Examiner has not provided evidence to the contrary, it is agreed that no evidence disputing differences in phenotypic effect for various null alleles of a specific gene has been made of record. However, with respect to the rejection at hand, a multitude of references from the art and from the specification support that differences in genetic background affect the resulting phenotype of the mice encompassed by the claims (for example refer to the specification at page 53, lines 16-21; page 54, line 8 and lines 13-15; refer to pages 6-8 of the office action mailed 11/06/2003 and the references contained therein). Finally, the excerpt of Bilkei-wGorzo is replete with statements regarding the differences in performance of mice comprising the same gene disruption on different genetic backgrounds as well as differences in the effects of pharmaceuticals on the

different genetic backgrounds. In fact, Applicant has underlined the statement in an excerpt from Bilkei-Gorzo that reads "the expressivity of the mutant phenotype was strongly dependent on the behavioral paradigm and on the genetic background". It is clear from the specification and the art of record, that the genetic background of the mice has an effect on the phenotype of the mice as claimed and that the claimed phenotypes do not arise in all genetic backgrounds encompassed by the claims. Therefore, the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

Joe Woitach
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